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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/582,486	11/16/2000	Christopher Joseph Schofield	P02005US0	3471

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EXAMINER

BORIN, MICHAEL L

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 05/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/582,486	Applicant(s) SCHOFIELD ET AL.	
	Examiner Michael Borin	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 March 2005.
 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 235 and 236 is/are pending in the application.
 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
 5) ☐ Claim(s) _____ is/are allowed.
 6) ☒ Claim(s) 235, 236 is/are rejected.
 7) ☐ Claim(s) _____ is/are objected to.
 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 03/21/2005 has been entered.

Status of claims

2. All previously pending claims are canceled. Claims 235, 236 are added.

The claims are addressed to the extent they read on the elected species - DAOCS comprising modification of Leu158 residue.

3. Rejections not reiterated from previous Office actions are hereby withdrawn. The following rejections and objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112, second paragraph.

4. Claims 235,236 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 235 is directed to a DAOCS enzyme having modifications which are "equivalent" to positions in protein SEQ ID No. 1. It is not clear what positions are

“equivalent” in proteins other than protein SEQ ID No. 1; the specification does not define metes and bounds of the term.

Applicant points at Fig. 3 in newly submitted reference of Kovacevic et al. This figure compares structures of DAOCS from *S. clavuligerus* of SEQ ID No. 1 with DAOCS/DACs enzyme from another organism. At best, the figure demonstrates correlation for sequence of enzymes from these two organisms. It does not identify “core structure” common for DAOCS enzymes – which belong to an extensive family of proteins (see specification, pages 1-2) – that would provide a correlation between structures of DAOCS enzymes of different origin and identify what positions are “equivalent” in proteins other than protein SEQ ID No. 1. Contrary, as sequence alignment in Kovacevic et al. is not a direct alignment, but is rather achieved by shifting sequences, such shifted alignment illustrates the need for guidance on identifying “equivalent” positions for other DAOCS enzymes. Note that the same sequence of Kovacevic et al., if aligned directly with SEQ ID No. 1, could, and in fact has been, used as an art teaching substitutions as instantly claimed.

B. Claim 236: The language “ Enzyme ... comprising substitutions at positions 158 and 304 of SEQ ID No. 1” is unclear. Does it mean protein SEQ ID No. 1 comprising substitutions at said positions, or protein similar to protein SEQ ID No. 1 (as in claim 235) in which positions corresponding to said positions in SEQ ID No. 1 are substituted? The latter is assumed in the following rejections.

Claim Rejections - 35 USC § 112, first paragraph (enablement).

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5. Claims 235,236 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the particular DAOCS of SEQ ID No. 1, does not reasonably provide enablement for any other DAOCS having substitutions at "equivalent" positions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The only structure of a DAOCS enzyme demonstrated in specification is the structure of DAOCS from *S. clavuligerus* of SEQ ID No. 1. There is no indication that any other "DAOCS enzyme" has same residues. Neither binding site nor any other residues have been identified to any DAOCS other than DAOCS from *S. clavuligerus* of SEQ ID No. 1. There is no guidance on how to identify binding site and/or "equivalent" residues in other DAOCS enzymes. Figure 2, addressed previously by applicant, reflects binding site for penicillin nucleus, not binding site for penicillin side chain and does not guide on how to identify binding site and/or particular residues in other DAOCS enzymes. Hence, the claims are not clear as to which residues are to be substituted for residues 158 and 304 in SEQ ID No. 1.

With respect to reference of Kovacevic et al., addressed by applicants, this reference compares structures of DAOCS from *S. clavuligerus* of SEQ ID No. 1 with DAOCS/DACs enzyme from another organism. At best, the figure demonstrates correlation for sequence of enzymes from these two organisms. It does not identify "core structure" common for DAOCS enzymes – which belong to an extensive family of proteins (see specification, pages 1-2) – that would provide a correlation between structures of DAOCS enzymes of different origin and identify what positions are

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"equivalent" in proteins other than protein SEQ ID No. 1. Contrary, as discussed in rejection under 112, second paragraph above, Kovacevic et al. reference demonstrates the need for guidance in identifying "equivalent" residues, because, depending on aligning of sequences, the sequence in the reference can be used as either demonstration of "equivalent" residues, or as art teaching substitutions exactly as instantly claimed.

With respect to further publications of other researchers, as stated in the preceding Office action, the enablement sufficiency of a specification is determined as of filing date and can not be demonstrated by submitting later publications. *Hybritech, Inc. V. Monoclonal antibodies, Inc.*, 231 USPQ 81 (Fed. Cir. 1986)

Claim Rejections - 35 USC § 112, first paragraph (written description, new matter).

7. Claim 235 is rejected under 35 .S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Claim 235 introduces new matter as it addresses substitution of residues which are equivalent to Leu158 and Asn304. While specification teaches substitutions of these exact residues, it does not disclose substitution in positions which are "equivalent".

Claim Rejections - 35 USC 102.

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The following is a quotation of the appropriate paragraphs of 35 U.S.C.102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.


7. Claims 235,236 are rejected under 35 U.S.C. 102(b) as being anticipated by Accession Numbers of Database Pir_76: S40253, S54101. The references and sequence alignment were provided in the first Office action on merits. The referenced sequences are sequences of DAOCS in which residues "equivalent" to Leu158 and Asn 304 in SEQ ID No. 1 are substituted with "V" (for Leu158) and "T" or "E" residues, respectively.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. The examiner can normally be reached on 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

 Michael Borin, Ph.D.
Primary Examiner
Art Unit 1631

mlb

5/20/05